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(54) TREATMENT PROCESS FOR PROMOTING WEIGHT LOSS EMPLOYING A SUBSTITUTED DELTA 5-ANDROSTENE

BEHANDLUNGSVERFAHREN ZUR FÖRDERUNG DES GEWICHTSVERLUSTES UNTER VERWENDUNG EINES SUBSTITUIERTEN DELTA-5-ANDROSTENS

PROCEDE DE TRAITEMENT FAVORISANT LA PERTE DE POIDS, EMPLOYANT DELTA 5-ANDROSTENE SUBSTITUE

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Description

Field of the Invention

[0001] Broadly, the invention relates to the use of steroids for effecting a desired biological response. Specifically, the invention relates to the use of a substituted dehydroepiandrosterone capable of effecting a variety of beneficial biological responses without inducing the formation of androgen and estrogen hormones which is commonly associated with dehydroepiandrosterone treatment.

Background

[0002] Dehydroepiandrosterone (Δ5-androstene 3β-hydroxy, 17-one) (hereinafter referenced as DHEA) is a natural steroid produced in the adrenal glands, testes and brain. Dehydroepiandrosterone is an intermediate in the Dehydroepiandrosterone is an intermediate in the biosynthetic production of estrogen and androgen (sex hormones) from 17α-hydroxy pregnenolone.

[0003] Treatment with DHEA is believed to stimulate various biological responses including promoting weight loss and inducing an increase in the production of the sex hormones androgen and estrogen.

[0004] The ability of DHEA to promote weight control is believed to be mediated through enhanced thermogenesis (conversion to heat energy rather than chemical energy such as ATP and/or triacylglycerides). The thermogenic effect of DHEA is believed to result from a simulation in the synthesis of liver thermogenic enzymes such as mitochondrial glycerol 3-phosphate dehydrogenase (G3P-DH) and cytosolic malic enzyme (ME) which tend to reduce the efficiency of energy metabolism.

[0005] Unfortunately, DHEA is not useful as a therapeutic agent for controlling weight gain/promoting weight loss because the dose rate of DHEA necessary to achieve these desired characteristics may also stimulate the production of sex hormones which is associated with various undesired side effects.

[0006] US-A 4,898,694 describes steroid permutations of a general very broad formula which can be used e.g. as anti-cancer, anti-obesity, anti-diabetic agents. In the same context EP 0 133 995 discloses different steroids and therapeutic compositions again falling under a very broad general formula. In both cases it can be doubted that each substance covered by the formulae actually has the effect noted in the references.

[0007] Accordingly, a therapeutic agent possessing the weight loss characteristic of DHEA without the associated sex hormone stimulating characteristic would be extremely useful.

Summary of the Invention

[0008] A method for controlling weight gain and/or promoting weight loss which includes the step of treating a subject with an effective weight gain controlling and/or weight loss promoting amount of a substituted Δ5-Androstene effective for stimulating the desired biological response while ineffective for inducing the synthesis of sex hormones.

[0009] Steroids believed to provide the desired beneficial biological results include:

Δ5-Androstene-3β-ol-7,17-dione
Δ5-Androstene-3β-17β-diol-7-one

and derivatives thereof wherein (i) at least one of the hydroxyl groups is esterified with an acid selected from the group consisting of (i) C_{2-22} aliphatic acids that may or may not contain one or more double bonds and may or may not contain branched carbon chains, (ii) C_{7-12} aromatic acids, (iii) C_3 or larger dicarboxylic acids in which only one of the carboxyl groups is esterified to the hydroxyl group(s) on the steroid leaving the second carboxyl group free or in the form of a salt, or (iv) inorganic acids such as sulfuric and phosphoric.

[0010] These steroids may also be administered as carbamate, enanthates and other derivatives capable of releasing the free steroid in the intestinal tract, the blood or in tissues. The desired biological activity is a function of the steroid moiety. Derivation of the moiety may serve a variety of possible functions including stabilization of the steroid, flavoring or obscuring the natural flavor of the steroid, or affecting the rate of absorption of the steroid.

Detailed Description of the Invention Including a Best Mode

[0011] Δ5-Androstene substituted at C-3, C-7 and/or C-17 with a hydroxyl or keto group are biologically effective for controlling weight gain and promoting weight loss without substantial stimulation in the production of sex hormones. Derivatives of these substituted Δ5-Androstene in which at least one of the hydroxyl groups is esterified with an acid selected from the group consisting of (i) C_{2-22} aliphatic acids that may or may not contain one or more double bonds

and may or may not contain branched carbon chains, (ii) C_{7-12} aromatic acids, (iii) C_3 or larger dicarboxylic acids in which only one of the carboxyl groups is esterified to they hydroxyl group(s) on the steroid leaving the second carboxyl group free or in the form of a salt, or (iv) inorganic acids such as sulfuric and phosphoric, and also believed to possess the desired characteristics.

[0012] These steroids may also be administered as carbamate, enanthates and other derivatives capable of releasing the free steroid in the intestinal tract, the blood or in tissues. The desired biological activity is a function of the steroid moiety; the derivatizing moiety may serve to stabilize the steroid,to favor or to retard absorption or to obscure its flavor.

Synthesis

Δ5-Androstene-3β-ol 7,17-dione (7-keto DHEA)

[0013] Δ5-Androstene 3β-ol, 7,17-dione can be synthesized from commercially available DHEA acetate by sequentially synthesizing:

3β-acetoxy-Δ5-androstene-17-one
3β-acetoxy-Δ5-androstene-7,17-one
Δ5-androstene 3β-hydroxy-7,17-one

[0014] 3β-acetoxy-Δ5-androstene-7,17-one (7-one DHEA acetate) can be synthesized from 3β-acetoxy-A5-androstene-17-one (DHEA acetate) by reacting the DHEA acetate with the oxidizing agent CrO_3 in accordance with the procedure outlined in Fieser, L.F., Jour. Am. Chem. Soc., vol. 75, pp 4386-4394 (1953).

[0015] Δ5-androstene 3β-hydroxy-7,17-dione (7-one DHEA) can be synthesized from the 7-one acetate and purified by employing the deesterification and purification steps set forth above with respect to the synthesis and purification of 7-hydroxy DHEA from 7-hydroxy DHEA diacetate.

Δ5-Androstene 3β,17β-diol, 7-one (7-keto Androstenediol)

[0016] Δ5-Androstene 3β,17β-diol-7-one can be synthesized from commercially available androstenediol diacetate by sequentially synthesizing:

Δ5-androstene 3β,17β-diol diacetate
Δ5-androstene 3β,17β-diol-7-one diacetate
Δ5-androstene 3β,17β-diol-7-one

[0017] Δ5-androstene 3β,17β-diol-7-one diacetate can be synthesized from Δ5-androstene 3β,17β-diol diacetate (Androstenediol diacetate) by reacting the androstenediol diacetate with the oxidizing agent CrO_3 in accordance with the procedure outlined in Fieser, L.F., Jour. Am. Chem. Soc., vol. 75, pp 4386-4394 (1953).

[0018] Δ5-androstene 3β,17β-diol-7-one (7-one androstenediol) can be synthesized from Δ5-androstene 3β,17β-diol-7-one diacetate and purified by employing the deesterification and purification steps set forth above with respect to the synthesis and purification of 7-hydroxy DHEA from 7-hydroxy DHEA diacetate.

[0019] Without intending to be unduly limited thereby, it is believed that the substituted Δ5-Androstene may be further modified by esterifying one or more of the hydroxyl groups with any of a variety of organic acids and inorganic acids such as sulfuric or phosphoric acid.

Treatment

[0020] A subject may be treated with the substituted Δ5-Androstene by any of the commonly accepted practices including orally or by injection. It is believed that treatment at a dosage rate of about 0.1 to 2 grams, preferably about 0.5 to 2 grams, steroid per 100 kilograms body weight per day is generally effective for promoting weight loss and/or preventing weight gain. A dose rate of less than 0.1 gam per 100 kilograms bodyweight is believed to be generally ineffective for preventing weight gain wile a dose rate of greater than about 2 grams per 100 kilograms bodyweight increases the cost of the treatment without providing a corresponding benefit in performance. The optimum dose rate to be administered to a subject is case specific as the optimum dose rate depends upon several factors including current body composition (percent fat), the desired effect (weight gain prevention versus weight loss), eating habits of the individual (daily caloric intake), and the like. As would be expected, the dose rate provided to a subject for the purpose of promoting weight loss will be greater than that necessary to promote weight maintenance assuming identical caloric intake under each program.

[0021] Without intending to be limited thereby, we believe that the substituted Δ5-Androstene are metabolic intermediates between the conversion of DHEA to a intermediate between the conversion of DHEA to a metabolite(s) actually responsible for enhancing the production of thermogenic enzymes such as glycerol 3-phosphate dehydrogenase and malic enzyme.

[0022] The subject may be treated with a steroid on any desired schedule. It is anticipated that the steroid will be effective for preventing weight gain and/or promoting weight loss not only while actively present within the body, but also for as long as the concentration of the induced thermogenic enzyme(s) remain elevated. At the present time, the duration of effectiveness for the steroid is not fully appreciated. However, it is believed that the steroid is not stored within the body and will be substantially removed and/or deactivated within days after administration. Accordingly, the subject should be conveniently treated every day for optimum performance but may be treated less frequency such as every other day or week when less than maximum performance is acceptable. For example, a subject placed on a weight maintenance program may require treatment with the steroid thermogenic enzyme(s) are not retained during the entire period between treatments as the weight loss occurring within the first few days after treatment counterbalances any weight gain. occurring during the remaining days between treatments.

[0023] As is apparent from the factors which affect dosage and dose rate, each particular subject should be carefully and frequently reviewed and the dosage and/or dose rate altered in accordance with the particular situation.

Experimental

Example I

Synthesis Δ5-Androstene 3β-ol-7,17-dione

[0024] (*Step 1*) Into a 50 ml flask equipped with a magnetic stirrer and a water bath was placed 6.5 ml acetic anhydride, 23 ml acetic acid, 1.7 grams sodium acetate, and 2 grams DHEA acetate to form a first mixture. Into the first mixture was added 2 grams chromium trioxide over a thirty minute period to form a second mixture. The first mixture was maintained at a constant temperature of 56-58°C and continuously agitated during addition of the chromium trioxide. The second mixture was maintained at 56-58°C and continuously agitated for an additional hour after which the second mixture was cooled and slowly poured under continuous agitation into 600 ml of ice water to form a precipitate. The flocculent precipitate was collected on a sintered glass funnel and washed with water until no longer green. After drying in vacuo over P_2O_5 the product was dissolved in methanol and recrystallized to yield substantially pure Δ5-Androstene 3β-acetoxy-7,17-dione having a melting point of about 191-192°C.

[0025] (*Step 2*) The precipitate was resolubilized in 500 ml of methanol in a one liter, triple necked, round bottom flask equipped with a magnetic stirrer and reflux condenser to form a third solution. The third solution was placed under a N_2 atmosphere and heated under constant agitation to reflux. Into the third solution was added 250 ml of a 5% solution of Na_2CO_3 to form a fourth solution. The fourth solution was refluxed under constant agitation for 45 minutes. The methanol was rotovapped off and the aqueous fourth solution carefully brought to a pH of 7 with an appropriate amount of glacial acetic acid. The neutralized fourth solution was extracted with two 100 ml portions of dichloromethane, and two portions combined, and the dichloromethane evaporated in vacuo. The extracted solids were then azeotropically dried first with absolute ethanol and then with two separate portions of acetone. Methanol was added to the dried extracted solids until the solids were completely dissolved to form a fifth solution. Hexane was added to the fifth solution until the solution began to cloud at which time crystals of Δ5-Androstene 3β-ol-7,17-dione began to form at room temperature.

[0026] A second crop of Δ5-Androstene 3β-ol-7,17-dione crystals was obtained by cooling the remaining sixth solution.

[0027] The resultant product had a melting point of about 235-238°C.

Example II

Synthesis Δ5-Androstene 3β,17(β)-diol-7-one

[0028] *(Step 1)* Into a 50 ml flask equipped with a magnetic stirrer and a water bath was placed 6.5 ml acetic anhydride, 23 ml acetic acid, 1.7 grams sodium acetate, and 2 grams androstenediol diacetate to form a first mixture. Into the first mixture was added 2 grams chromium trioxide over a thirty minute period to form a second mixture. The first mixture was maintained at a constant temperature of 56-58°C and continuously agitated during addition of the chromium trioxide. The second mixture was maintained at 56-58°C and continuously agitated for an additional hour after which the second mixture was cooled and slowly poured under continuous agitation into 600 ml of ice water to form a precipitate. The flocculent precipitate was filtered through a sintered glass funnel, washed with water until no longer green and

dried in vacuo.

[0029] (*Step 2*) The dried precipitate was resolubilized in 500 ml of methanol in a one liter, round bottom flask equipped with a magnetic stirrer and reflux condenser to form a third solution. The third solution was placed under a N_2 atmosphere and heated under constant agitation to reflux. Into the third solution was added 250 ml of a 5% aqueous solution of Na_2CO_3 to form a fourth solution. The fourth solution was refluxed under constant agitation for 45 minutes. The methanol was rotovapped off and the aqueous fourth solution carefully brought to a pH of 7 with an appropriate amount of glacial acetic acid. The neutralized fourth solution was extracted twice with 100 ml portions of dichloromethane and the combined extract evaporated in vacuo. The extracted solids were then azeotropically dried first with absolute ethanol and then twice with acetone. Methanol was added to the dried extracted solids until the solids were completely dissolved to form a fifth solution. Hexane was added to the fifth solution until the solution began to cloud at which time crystals of Δ5-Androstene 3β17β-diol-7-one began to form at room temperature.

[0030] The resultant product had a melting point of about 200-202°C.

Example III

Enzymatic Activity Protocol

[0031] Administration of Hormone: Male Sprague Dawley rats weighing 125-150 gm were obtained from Sasco Inc. of Oregon, WI. The rats were allowed free access to water and Purina Rat Chow pellets for the first day after arrival. Administration of the steroids began on day two. The steroids were either administered orally (combined with the Purina Rat Chow) or injected intraperitoneal as set forth in Table 1 for 6 days.

Preparation of Liver Mitochondria and Cytosol. The treated rats were sacrificed by decapitation after 6 days of treatment. The livers were excised, placed in 10 ml of a buffer consisting of 250 mM mannitol, 70 mM sucrose, and 3 mM Hepes (hereinafter MSH buffer) at pH 7.4, weighted, removed from the buffer, minced with scissors, washed with MSH buffer, suspended in MSH buffer at a ratio of 1 gram minced liver to 5 ml MSH buffer at a ratio of 1 gram minced liver to 5 ml MSH buffer, and homogenized with a Potter-Elvehjem rotary homogenizer.

[0032] The Mitochondria fraction was prepared by the method described in Johnson, D. and Lardy, H.A., Methods Enzymology, vol. 10, pp 94-96 (1967) which is hereby incorporated by reference. Briefly, liver homogenate was centrifuged in a Beckman Model J2-21 centrifuge, JA-20 rotor at 750g for 10 minutes and the resulting supernatant solution centrifuged at 15,000g for an additional 10 minutes. The resulting mitochondrial pellets were washed twice with MSH buffer, resuspended in 0.8 to 1 ml of a 35 wt% aqueous glycerol solution, and stored at -70°C.

[0033] The Cytosolic fraction was obtained by recentrifuging the previously centrifuged supernatant solution at 100,000g for 30 minutes in a Beckman Model L2 ultracentrifuge, type 40 rotor. The resultant supernatant solution was stored at -70°C.

[0034] Protein concentrations in the resultant preparations were determined by the Biuret method described in Layne E., Methods Enzymology, vol. 3, pp 450451 (1957) which is hereby incorporated by reference. Briefly, the protein concentrations were determined by treating a dilute protein solution with copper tartrate solution and measuring the optical density at 540 nm.

[0035] Enzyme Assays. Mitochondrial G3P-DH activity was measured by the method described in Wernette, M.E., Ochs, R.S., and Lardy, H.A., J. Biol. Chem., vol. 256, pp 12767-12771 (1981) which is a modified version of the method described in Gardner, R.S., Anal. Biochem., vol. 59, pp 272-276 (1974). Both references are hereby incorporated by reference. Briefly, aliquots of the previously prepared mitochondria containing 0.1 to 0.2 mg of protein were incubated in a test tube containing 50 mM sn-glycerol-3-P, 50 mM potassium phosphate (pH 7.0), 1 mM KCN, and 0.2% p-iodonitrotetrazolium violet in a total volume of 0.4 ml for 30 minutes at 37°C. The incubating mitochondria were continuously agitated during the incubation period by a Dubnoff shaker agitated at 100 cycles/min. Incubation was ceased by the addition of 0.6 ml of 1 M acetic acid to the test tube. The iodoformazan formed during the incubation period was extracted into 2 ml of ethyl acetate by adding the ethyl acetate to the test tube, mixing thoroughly, then decanting the ethyl acetate containing the iodoformazan from the test tube. The optical densities of the iodoformazan containing ethyl acetate layers were read at 490 nm by means of an On Line Instrument Systems, Model 3820 Data System, Spectrophotometry, Cary - 15, Version 4.08. An extinction coefficient value of 2.01×10^4/(M cm) for the iodoformazan product in ethyl acetate was used to calculate enzyme activities.

[0036] Cytosolic malic enzyme activity was measured in accordance with the method described in Hsu, R.Y. and Lardy, H.A., Methods Enzymol., vol. 8, pp 230-235 (1967). Briefly, aliquots of the previously prepared cytosol containing 0.1 to 0.5 mg of protein were incubated in a test tube containing 0.8 mM malate, 67 mM triethanolamine buffer (pH 7.4), 4 mM $MnCl_2$, and 0.2 mM NADP in a total volume of 1 ml for 3 min at 26°C. the incubating cytosol was continuously agitated during the incubation period by a Dubnoff shaker agitated at 100 cycles/min. Activity of malic enzyme was calculated from the rate of change in optical density measured at 340 nm from 0.5 to 2 minutes with an On Line Instrument Systems, Model 3820 Data System, Spectrophotometry, Cary - 15, version 4.08.

[0037] Results of several tests conducted in accordance with the protocol established above are set forth in Table 1.

Table 1

(Enzyme induction in rat liver by C_{19} steroids)

Steroids		# rats	wt % steroid in diet	G3P-DH (% control[1])	Malic Enzyme (% control[1])
Δ5 Androstene 3β-ol-17-one	(DHEA)	1	0.2	380	512
		29	0.1	265	---
		27	0.1	---	394
		12	0.05	251	337
		3	0.01	139	64
Δ5 Androstene 3β,7α-ol-17-one	(7α-dihydroxy DHEA)	2	0.05	292	423
		2	0.033	308	374
Δ5 Androstene 3β,7α,19-ol-17-one	(7α,19-dihydroxy DHEA)	3	0.1	117	118
Δ5-Androstene 3β-ol-7,17-one	(7-keto DHEA)	3	0.1	220	350
		5	0.05	439	449
		2	0.0575	224	341
		3	0.01	183	229
Δ5-Androstene-3β-ol-7,17-one acetate	(7-keto DHEA acetate)	3	0.115	261	447
Δ5-Androstene 3β-ol-7-methyl-17-one	(7-methyl DHEA)	3	0.1	91	121
Δ5-Androstene 3β,7α,17β-triol		2	0.1	227	611
		2	0.01	99	108
Δ5-Androstene 3β-17β-diol-7-one		2	0.1	286	1030
		3	0.05	360	305
		4	0.01	180	175
Δ5-Androstene 3β,17β-diol 7-one diacetate		3	0.13	232	452
		2	0.01	173	119

[1] Control activity based upon enzyme activity in the livers of rats fed with the stock diet without hormone supplement. IN each assay control rats fed only stock diet without hormone supplement were compared with test rats fed stock diet supplement with indicated wt% hormone.

Claims

1. A biologically active steroid effective for inhibiting weight gain in a subject without substantially promoting the synthesis of sex hormones, comprising a steroid selected from the group consisting of derivatives of Δ5-Androstene 3β, 17β diol-7 one capable of releasing the free steroid in the intestinal tract, blood or tissues.

2. A biologically active steroid according to claim 1, in which at least one of the hydroxyl groups of Δ5-Androstene 3β, 17β diol-7 one is esterified with an acid selected from the group consisting of (i) C_2 to C_{22} aliphatic acids, (ii) C_{7-12} aromatic acids, (iii) C_3 or greater dicarboxylic acids in which only one of the carboxyl groups is esterified to the hydroxyl group(s) on the steroid, or (iv) inorganic acids.

3. A biologically active steroid according to claim 1, being provided as carbamate or enanthate.

4. A biologically active steroid according to claims 1-3, for inhibiting weight gain in a mammal, especially a human.

5. Pharmaceutical composition effective for inhibiting weight gain in a subject which can be administered to the subject by usual practices, comprising Δ5-Androstene 3β, 17β diol-7 one or derivatives thereof capable of releasing the free steroid in the intestinal tract, blood or tissues and any further substance necessary for the selected mode of administration.

6. Pharmaceutical composition according to claim 5, being intended for inhibiting weight gain in a mammal, especially a human.

7. Use of a steroid selected from the group consisting of Δ5-Androstene 3β-hydroxy-7, 17 dione and derivatives thereof capable of releasing the free steroid in the intestinal tract, blood or tissues for the manufacture of a product for inhibiting weight gain without substantially promoting the synthesis of sex hormones.

8. Use of a steroid selected from the group consisting of derivatives of Δ5-Androstene 3β-hydroxy-7, 17 dione, in which at least one of the hydroxyl groups is esterified with an acid selected from the group consisting of (i) C_2 to C_{22} aliphatic acids, (ii) C_{7-12} aromatic acids, (iii) C_3 or greater dicarboxylic acids in which only one of the carboxyl groups is esterified to the hydroxyl group(s) on the steroid, or (iv) inorganic acids, for the manufacture of a product for inhibiting weight gain without substantially promoting the synthesis of sex hormones.

9. Use of a steroid selected from the group consisting of derivatives of Δ5-Androstene 3β-hydroxy-7, 17 dione, said derivative being provided as carbamate or enanthate, for the manufacture of a product for inhibiting weight gain without substantially promoting the synthesis of sex hormones.

10. Use of a steroid selected from the group consisting of Δ5-Androstene-3β-7α,17-triol or Δ5-Androstene-3β 7, 17-triol, for the manufacture of a product for inhibiting weight gain without substantially promoting the synthesis of sex hormones.

Patentansprüche

1. Biologisch aktives Steroid, das zur Verhinderung einer Gewichtszunahme bei einer Person wirkt, ohne im wesentlichen die Synthese von Sexualhormonen zu fördern, mit einem Steroid, das ausgewählt ist aus der Gruppe bestehend aus Derivaten von Δ5-Androsten-3β, 17β-diol-7-on, die das freie Steroid im Verdauungstrakt, im Blut oder in Geweben freisetzen können.

2. Biologisch aktives Steroid nach Anspruch 1, wobei mindestens eine von den Hydroxylgruppen von Δ5-Androsten-3β, 17β-diol-7-on mit einer Säure verestert wird, die ausgewählt ist aus der Gruppe bestehend aus (i) aliphatischen C_2- bis C_{22}-Säuren, (ii) aromatischen C_{7-12}-Säuren, (iii) $C_{3\ \text{oder mehr}}$-Dicarbonsäuren, wobei nur eine von den Carboxylgruppen an dem Steroid zu der/den Hydroxylgruppe(n) verestert ist, oder (iv) anorganischen Säuren.

3. Biologisch aktives Steroid nach Anspruch 1, das als Carbamat oder Enantat vorgesehen ist.

4. Biologisch aktives Steroid nach den Ansprüchen 1 - 3 zum Verhindern einer Gewichtszunahme bei einem Säugetier, insbesondere einem Menschen.

5. Pharmazeutische Zusammensetzung, die zum Verhindern einer Gewichtszunahme bei einer Person wirksam ist und der Person mit üblichen Praktiken verabreicht werden kann, mit A5-Androsten-3β,17β-diol-7-on oder Derivaten desselben, die das freie Steroid im Verdauungstrakt, im Blut oder in Geweben freisetzen können, und mit jeder weiteren für die gewählte Verabreichungsweise notwendigen Substanz.

6. Pharmazeutische Zusammensetzung nach Anspruch 5, vorgesehen zum Verhindern einer Gewichtszunahme bei einem Säugetier, insbesondere einem Menschen.

7. Verwendung eines Steroids, das ausgewählt ist aus der Gruppe bestehend aus Δ5-Androsten-3β-hydroxy-7, 17-dion und Derivaten desselben, die das freie Steroid im Verdauungstrakt, im Blut oder in Geweben freisetzen können, zur Herstellung eines Produkts zum Verhindern einer Gewichtszunahme, ohne im wesentlichen die Synthese von Sexualhormonen zu fördern.

8. Verwendung eines Steroids, das ausgewählt ist aus der Gruppe bestehend aus Derivaten von Δ5-Androsten-3β-hydroxy-7, 17-dion, wobei mindestens eine von den Hydroxylgruppen mit einer Säure verestert wird, die ausgewählt ist aus der Gruppe bestehend aus (i) aliphatischen C_2- bis C_{22}-Säuren, (ii) aromatischen C_{7-12}-Säuren, (iii) $C_{3\ oder\ mehr}$-Dicarbonsäuren, wobei nur eine von den Carboxylgruppen zu der/den Hydroxylgruppe(n) an dem Steroid verestert ist, oder (iv) anorganischen Säuren, zur Herstellung eines Produkts zum Verhindern einer Gewichtszunahme, ohne im wesentlichen die Synthese von Sexualhormonen zu fördern.

9. Verwendung eines Steroids, das ausgewählt ist aus der Gruppe bestehend aus Derivaten von A5-Androsten-3β-hydroxy-7, 17-dion, wobei das Derivat als Carbamat oder Enantat vorgesehen ist, zur Herstellung eines Produkts zum Verhindern einer Gewichtszunahme, ohne im wesentlichen die Synthese von Sexualhormonen zu fördern.

10. Verwendung eines Steroids, das ausgewählt ist aus der Gruppe bestehend aus Δ5-Androsten-3β-7α-17-triol oder Δ5-Androsten-3β-7,17-triol, zur Herstellung eines Produkts zum Verhindern einer Gewichtszunahme, ohne im wesentlichen die Synthese von Sexualhormonen zu fördern.

Revendications

1. Un stéroïde biologiquement actif efficace pour inhiber le gain de poids chez un sujet, sans activer notablement la synthèse d'hormones sexuelles, comprenant un stéroïde choisi dans la classe formée par les dérivés de Δ5-androstène-3β,17β-diol-7-one capables de libérer le stéroïde libre dans les voies intestinales, le sang ou des tissus.

2. Un stéroïde biologiquement actif selon la revendication 1, dans lequel au moins l'un des groupes hydroxyle de la Δ5-androstène-3β,17β-diol-7-one est estérifié par un acide choisi dans la classe formée par (i) les acides aliphatiques en C_2 à C_{22}, (ii) les acides aromatiques en C_7 à C_{12}, (iii) les acides dicarboxyliques en C_3 ou plus dans lesquels un seul des groupes carboxyle forme un ester avec le ou les groupes hydroxyle du stéroïde, ou (iv) les acides minéraux.

3. Un stéroïde biologiquement actif selon la revendication 1, qui est fourni sous forme de carbamate ou d'oenanthate.

4. Un stéroïde biologiquement actif selon les revendications 1 à 3, pour inhiber le gain de poids chez un mammifère, notamment un être humain.

5. Composition pharmaceutique efficace pour inhiber le gain de poids chez un sujet, qui peut être administrée au sujet par des pratiques usuelles, comprenant de la Δ5-androstène-3β,17β-diol-7-one ou des dérivés de celle-ci qui sont capables de libérer le stéroïde libre dans les voies intestinales, le sang ou des tissus, et toute autre substance nécessaire pour le mode d'administration choisi.

6. Composition pharmaceutique selon la revendication 5, qui est destinée à inhiber le gain de poids chez un mammifère, notamment un être humain.

7. Utilisation d'un stéroïde choisi dans la classe formée par la Δ5-androstène-3β-hydroxy-7,17-dione et ses dérivés capables de libérer le stéroïde libre dans les voies intestinales, le sang ou des tissus, pour la fabrication d'un produit destiné à inhiber le gain de poids sans activer notablement la synthèse d'hormones sexuelles.

8. Utilisation d'un stéroïde choisi dans la classe formée par les dérivés de Δ5-androstène-3β-hydroxy-7,17-dione dans lesquels au moins l'un des groupes hydroxyle est estérifié par un acide choisi dans la classe formée par (i) les acides aliphatiques en C_2 à C_{22}, (ii) les acides aromatiques en C_7 à C_{12}, (iii) les acides dicarboxyliques en C_3 ou plus dans lesquels un seul des groupes carboxyle forme un ester avec le ou les groupes hydroxyle du stéroïde, ou (iv) les acides minéraux, pour la fabrication d'un produit destiné à inhiber le gain de poids sans activer notablement la synthèse d'hormones sexuelles.

9. Utilisation d'un stéroïde choisi dans la classe formée par les dérivés de Δ5-androstène-3β-hydroxy-7,17-dione, ledit dérivé étant fourni sous forme de carbamate ou d'oenanthate, pour la fabrication d'un produit destiné à inhiber le gain de poids sans activer notablement la synthèse d'hormones sexuelles.

10. Utilisation d'un stéroïde choisi dans la classe formée par le Δ5-androstène-3β,7α,17-triol ou le Δ5-androstène-3β,7,17-triol, pour la fabrication d'un produit destiné à inhiber le gain de poids sans activer notablement la synthèse d'hormones sexuelles.